

Table of Evidence Supporting Enablement
U.S. Patent Application Number 09/392,862

<u>Data Source</u>	<u>Delivery Method</u>	<u>Delivery Vehicle</u>	<u>Fragment¹</u>	<u>Model System</u>	<u>Result</u>
Declaration of Dr. Gruenert (Item 6, p. 3-4)	In Vivo (nasal administration)	Lipofect-amine	786 bp containing wild type exon 10 of mCFTR	Animal model of cystic fibrosis: ΔF508	Successful in vivo gene therapy: functional correction of ion transport to normal ranges in immune competent mice
Prokopishyn et al., manuscript, "Targeted Genome Editing . . .", Exhibit A of 9/26/03	Ex Vivo (human umbilical cord blood stem/progenitor cells engrafted into mice)	Micro-injection	559 bp containing exons 1&2 of β ^S -globin gene	Sickle cell anemia: wild type β ^A -globin replaced w/ β ^S -globin mutation	Successful replacement and engraftment of corrected stem cells into immune deficient mice; replacement at both alleles; sufficient levels of gene conversion to support therapeutic benefit
Gonczi et al. manuscript, "Modification of Genomic . . .", Exhibit B of 9/26/03	In Vitro	Micro-injection	559 bp containing exons 1&2 of β ^S -globin mutation	Sickle cell anemia: wild type β ^A -globin replaced w/ β ^S -globin mutation	Successful & stable in vitro replacement of genomic DNA and successful mRNA expression
Gonczi et al. 2001, <i>Gene Therapy</i> 8:961-965, Exhibit C of 12/3/01	In Vivo (into lungs via intratracheal administration)	1. AVE 2. Lipofect-amine 3. DDAB	783 bp containing exon 10 of mCFTR w/ ΔF508	Animal model of cystic fibrosis: ΔF508	Successful in vivo fragment replacement and stable expression of altered DNA & mRNA
Kunzelmann et al. 1996, <i>Gene Therapy</i> 3:859-867, Exhibit D of 12/3/01	In Vitro (into cystic fibrosis epithelial cells)	1. Liposomes 2. Poly-amido-amine dendrimers	491 bp containing wild type exon 10 of CFTR	Cystic fibrosis: ΔF508	Successful replacement & correction of defect confirmed in genomic DNA and in mRNA; functional correction of ion transport confirmed by patch clamp
Gonczi et al. 1998, <i>Human Molecular Genetics</i> 7:1913-1919, Exhibit E of 12/3/01	In Vitro (into primary human airway epithelial cells)	1. Liposomes 2. Poly-amido-amine dendrimers	488 nt containing exon 10 of CFTR w/ ΔF508	Cystic fibrosis: ΔF508	Successful fragment replacement & correction of defect confirmed in genomic DNA and in mRNA
Kapsa et al. 2001, <i>Human Gene Therapy</i> 12:629-642, Exhibit F of 12/3/01	In Vivo (intramuscular injection) and In Vitro (applied to cultured cells)	1. Lipofect-amine 2. Lipofectin	603 bp containing exon 23 of dys gene	Animal model of Duchenne muscular dystrophy: <i>mdx</i>	Successful in vivo and in vitro replacement and correction of <i>mdx</i> dystrophin mutation in immune competent mice; shown to last up to 28 d in culture and at least 3 wks in vivo.
Gonczi et al. 2001, abstract, Technologies for <i>in situ</i> Repair . . ., Exhibit G of 12/3/01	In Vitro	Lipid-DNA complexes Micro-injection	Fragments containing β ^S -globin mutation	Sickle cell anemia: wild type β ^A -globin replaced w/ β ^S -globin mutation	Successful in vitro replacement at β-globin locus in hematopoietic cells; Replacement does not require transcription; Stable replacement lasts at least 5 wks

¹ Each fragment includes intronic sequence flanking the indicated exon(s).